

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT Rule 71.1)

Date of mailing
(day/month/year) 10.01.2002

Applicant's or agent's file reference
OO/20903

IMPORTANT NOTIFICATION

International application No.
PCT/IL00/00515

International filing date (day/month/year)
29/08/2000

Priority date (day/month/year)
01/09/1999

Applicant
YEDA RESEARCH AND DEVELOPMENT CO. LTD. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference OO/20903	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/IL00/00515	International filing date (<i>day/month/year</i>) 29/08/2000	Priority date (<i>day/month/year</i>) 01/09/1999
International Patent Classification (IPC) or national classification and IPC C12Q1/68		
Applicant YEDA RESEARCH AND DEVELOPMENT CO. LTD. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 6 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 09/03/2001	Date of completion of this report 10.01.2002
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer BROCHADO GARGANTA, M Telephone No. +49 89 2399 8935 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/IL00/00515

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-40 as originally filed

Claims, No.:

1-32 as originally filed

Drawings, sheets:

1/6-6/6 as originally filed

Sequence listing part of the description, pages:

1-12, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
☒ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

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International application No. PCT/IL00/00515

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 1-9,11-32
	No:	Claims 10
Inventive step (IS)	Yes:	Claims 1-6,11-32
	No:	Claims 7-10
Industrial applicability (IA)	Yes:	Claims 1-32
	No:	Claims

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

(A) MORONEY S E ET AL: 'ABORTIVE PRODUCTS AS INITIATING NUCLEOTIDES DURING TRANSCRIPTION BY T7 RNA POLYMERASE' BIOCHEMISTRY, vol. 30, no. 42, 1991, pages 10343-10349

(B) WO 98 23733 A

2. Novelty

2.1 The subject-matter of claims 1-9 and 11-32, relating to the use, methods and compositions using a template-dependent polymerase for incorporating at least a oligonucleotide triphosphate onto a nascent oligonucleotide-3'-OH in a template-dependent manner, is not known from the prior art and therefore these claims are considered to be novel (Article 33(2) PCT).

2.2 The subject-matter of claim 10, relating to a method for assaying a template-dependent polymerase for its activity in incorporating oligonucleotides triphosphates onto nascent oligonucleotide-3'-OH in a template-dependent manner, is not new in the sense of Article 33(2) PCT, because such a method is already disclosed in document A.

Document A discloses assaying the incorporation of di and trinucleotides into T7-RNA-polymerase, wherein it is concluded that both of them can only function as initiating nucleotides when complementary to the nucleotide sequence at promoter regions. However, a dinucleotide is not used as substrate for subsequent chain elongation in T7 RNA polymerase catalysed transcription reactions (see abstract).

3. Inventive step

3.1 Document B discloses the mutagenesis and screening for polymerase mutants with altered fidelity (see claim 1).

It would be within the capabilities of the skilled person to use the disclosed method for screening for polymerases having an increased activity in incorporating oligonucleotide triphosphates onto a nascent oligonucleotide-3'-OH, without for that needing to perform an inventive step. Thus, claim 7 is not considered to be based on an inventive concept (Article 33(3) PCT).

Claims 8 and 9 do not contain any additional features which in combination with the features of claim 7, meet the requirements of the PCT in respect of inventive step (Article 33(3) PCT). Their additional features are already disclosed in document A (see page 17, lines 13-23; page 18 and page 19).

3.2 As already stated in 2.2, it is disclosed in document A that di and trinucleotides can only function as initiating nucleotides when complementary to the nucleotide sequence at promoter regions. However, a dinucleotide (and perhaps a trinucleotide) cannot be used as substrate for subsequent chain elongation in T7 RNA polymerase catalysed transcription reactions (see abstract).

Therefore, the skilled person based on this teaching would never consider to incorporate the oligonucleotides onto a nascent oligonucleotide-3'-OH, as it would be for him obvious that it wouldn't work.

The use of oligonucleotide triphosphates by template-dependent polymerases, instead of, or in addition to, nucleotide triphosphates as basic building blocks or units for template-dependent synthesis, makes possible the creation of highly complex polymers having precisely locatable functional groups. Furthermore, while using relatively short oligonucleotide sequences as building blocks for template-dependent nucleic acid synthesis, not only the total number of building blocks required for synthesising a given nucleic acid sequence is reduced, but also each building block is less represented.

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EXAMINATION REPORT - SEPARATE SHEET**

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Thus, claims 1-6 and 11-32 are considered to be based on an inventive concept as required by Article 33(3) PCT.

Re Item VIII

Certain observations on the international application

1. The use of relative and subjective terms, like for example "novel" (claims 1 and 26) and better (claims 11 and 27) renders the claims unclear (Article 6 PCT), as these terms do not correspond to characterising features of the claimed methods but rather to subjective indications.
2. The use of general statements in the description which imply that the extent of protection may be expanded in some vague and not precisely defined way, is not allowable (see Guidelines III-4.3.a). Therefore the term "spirit of the invention" (page 36, line 8) has to be deleted (Article 6 PCT).